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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/356,322	SHALON ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9-18,21,23-27,29,32,34 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9-18,21,23-27,29,32,34 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 23 October 2007 in which the previous rejections were traversed. Applicant's arguments have been thoroughly reviewed and are discussed below.

The previous rejections in the Office Action dated 23 July 2007 are maintained.

Claims 7, 9-18, 21, 23-27, 29, 32, 34 and 39 are under prosecution.

Priority

reiterated from previous office action for purposes of consistency

2. Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, Parent Applications 08/514,875; 08/477,809; and 08/261,388 upon which priority is claimed do not provide adequate support under 35 U.S.C. 112 for claims 14, 29, 35 and 38-39 of this application. Instant Claims 14 and 29 are drawn to "covalently bound DNA"; These elements are not supported by the parent application cited above. Therefore the effective filing date for Claims 14 and 29 is the filing date of Application No. 08/688,488 i.e. 30 July 1996. The effective filing date for Claims 35, 38 and 39 is the filing date of parent application 08/514,875 i.e. 14 August 1995

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent

> or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 7, 9-18, 21, 23-27, 29-32, 34-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Fodor et al (U.S. Patent No. 6,610,482 filed 6 December 1990).

Regarding Claim 7, Fodor et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 1000 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length (Claims 40-43 & 56).

Regarding Claim 9, Fodor et al disclose the substrate wherein density is at least 2500 i.e. 10,000 regions/cm^2 (Claim 42).

Regarding Claim 10 Fodor et al disclose the substrate wherein the substrate is glass (Claim 61).

Regarding Claim 11 Fodor et al disclose the substrate wherein the substrate is non-porous i.e. glass (Claim 61).

Regarding Claim 12, Fodor et al disclose the substrate wherein the surface is hydrophobic e.g. plastics or hydrophobic linkers (Column 17, lines 14-48).

Regarding Claim 13, Fodor et al disclose the substrate wherein the surface comprises one or more functional groups e.g. silyl, hydroxyl, carboxyl, amine aldehyde, sulhydryl (Column 17, lines 24-29).

Regarding Claim 14, Fodor et al disclose the substrate wherein the DNA sequences are covalently bound (Column 8, lines 21-27).

Regarding Claim 15, Fodor et al disclose the substrate wherein the DNA sequences are non-covalently bound (Column 8, lines 21-27).

Regarding Claim 16, Fodor et al disclose the substrate wherein the DNA sequences are non-covalently bound (Column 8, lines 21-27) and the surface has cationic polymer on the surface (Column 18, lines 3-8).

Regarding Claim 17, Fodor et al disclose the substrate wherein the sequences are genomic DNA sequences (e.g. Column 85, lines 25-37).

Regarding Claim 18, Fodor et al disclose the substrate has at least 2500 or more regions i.e. 10,000/cm^2 (Claim 42).

Regarding Claim 21, Fodor et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 100 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length (Claims 40-43 & 56). Fodor et al does not teach the method steps recited in the claim. However, the method steps do not result in any structural or compositional difference over the substrate of Fodor. Furthermore, the courts have stated that the process of making a product does not distinguish the product over the prior art.

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113.

Regarding Claim 23, Fodor et al disclose the substrate wherein density is at least 2500 i.e. 10,000 regions/cm^2 (Claim 42).

Regarding Claim 24, Fodor et al disclose the substrate wherein the substrate is glass (Claim 61).

Regarding Claim 25, Fodor et al disclose the substrate wherein the substrate is non-porous i.e. glass (Claim 61).

Regarding Claim 26, Fodor et al disclose the substrate wherein the surface is hydrophobic e.g. plastics or hydrophobic linkers (Column 17, lines 14-48).

Regarding Claim 27, Fodor et al disclose the substrate wherein the surface comprises one or more functional groups e.g. silyl, hydroxyl, carboxyl, amine aldehyde, sulhydryl (Column 17, lines 24-29).

Regarding Claim 29, Fodor et al disclose the substrate wherein the DNA sequences are covalently bound (Column 8, lines 21-27).

Regarding Claim 30, Fodor et al disclose the substrate wherein the DNA sequences are non-covalently bound (Column 8, lines 21-27).

Regarding Claim 31, Fodor et al disclose the substrate wherein the sequences are genomic DNA sequences (e.g. Column 85, lines 25-37).

Regarding Claim 33, Fodor et al disclose the substrate has at least 10,000 regions (Claim 42).

Regarding Claim 34, Fodor et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 1000 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length and unique (i.e. different) in each region (Claims 40-43 & 56).

Regarding Claim 35, Fodor et al disclose the substrate of Claim 34. Fodor et al further teach the substrate is used for expression analysis (Column 66, lines 17-27). Fodor et al do not specifically teach detection of a two-fold change in abundance. However, the claimed detection is a recitation of intended use and the courts have stated that a recitation of intended use not distinguish a device over the prior art. Therefore, the detection does not further define the substrate of Claim 34.

A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987).

Regarding Claim 36, Fodor et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 1000 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length and unique (i.e. different) in each region (Claims 40-43 & 56). Fodor et al further teach the substrate wherein the DNA sequences are non-covalently bound

(Column 8, lines 21-27) and the surface has cationic polymer on the surface (Column 18, lines 3-8).

Regarding Claim 37, Fodor et al disclose the substrate wherein the DNA microarray is used to detect mRNA (e.g. Column 66, lines 17-27). Hence, the substrate comprises DNA complementary to mRNA i.e. cDNA.

Regarding Claim 38, Fodor et al disclose the substrate wherein the DNA is used to detect distinct gene sequences (e.g. Column 117). Fodor et al further teach the gene sequences have expression levels different for control vs test e.g. alleles (Column 117, lines 20-49).

Regarding Claim 39, Fodor et al disclose the substrate wherein the DNA is used to detect distinct gene sequences (e.g. Column 117). Fodor et al further teach the gene sequences have expression levels different for control vs test e.g. alleles (Column 117, lines 20-49).

Response to Arguments

5. Applicant asserts that Fodor does not teach a specific length of 50 subunits. In support of the assertion, Applicant points to Columns 2, line 2-23. The citation is noted but not sufficient to overcome the rejection. The passage cited by Applicant describes construction of an array having all possible probes of a preselected length. The cited passage does not teach or suggest probes of 50 nt cannot be synthesized. Nothing in the cited passage teaches or suggests that synthesis of 50-mers would be impossible or disadvantageous.

Applicant asserts that the effective filing date for the Fodor patent (U.S. Patent No. 6,610,482) should be later than June 25 1996. Applicant notes that the cover page of Fodor '482 identifies the patent as a continuation of U.S. Patent No. 6,197,506, which is a continuation of U.S. Patent No. 5,800,992. Applicant asserts that this is an error because the '482 patent contains 27 drawing sheets, whereas the earlier filed '506 and '992 patents only contains 2 drawings. From this Applicant asserts that '482 patent can only be a continuation-

in-part of the parent patents. The analysis has been considered but is not deemed persuasive. The '482 expressly incorporates by reference (first paragraph of the specification) all parent documents from which the drawing are taken. Furthermore, whether the '482 patent is a continuation-in-part or a continuation does not alter the facts that 1- the '482 patent is entitled to the effective filing date for all that the '992 patent teaches because the '482 properly claims priority to the '992 patent and 2- the entire teaching of the '992 patent is incorporated by reference in the '482 patent.

Applicant asserts that by the time of filing the '992 patent the Fodor group was working on VLSIPS technology, which could not have produced a microarray of polynucleotides each having more than 50 monomeric units." Applicant cites a passage from the '992 patent (cool 20-21) as support for the assertion. However, the cited passage merely teaches special complications to be considered when constructing an array of all possible probes of a defined length. The instant claims are drawn to arrays of 1,000 probes of 50 nucleotides. The '992 patent specifically teaches arrays of 50-mer probes (Column 20, lines 27-39 and Column 28, lines 40-43). While the instant claims encompass all-possible n-mers, the claims are not so limited as to require all possible probes of 50 nucleotides on the array. Because t=the instant claims are not limited to arrays having all possible 50-mers, any discussion of complete 50-mer arrays is not commensurate in scope with the claims. Applicant reiterates that a discussion of complete 50-mer arrays is relevant to the scope of the claims because the claim encompass the complete 50-mer array. It is maintained that the argument is not commensurate in scope with the instant claims because the claims merely require the presence of 50-mers, not all possible 50-mers.

Applicant further asserts that a discussion of complete n-mer arrays is relevant because the Fodor patent is interested in complete n-mer arrays. The argument is interesting, but is not persuasive because, the issue at hand is the scope of the instantly claimed invention. As

stated above the instant claims merely require the presence of probes having 50 nucleotides and the Fodor patent teaches arrays having probes of 50 nucleotides.

Applicant asserts that the only mention of probes having 50 nucleotides in the '992 patent is a passage at column 28 that describes hybridization. Applicant asserts that this passage does not describe an array of probes having 50 nucleotides. The assertion is noted, however careful reading of the passage clearly teaches use of their arrays wherein probes greater than 50 nucleotides are preferred:

> Much as in a Southern hybridization, the target and oligonucleotide probes are of lengths typically greater than about 25 nucleotides. Under appropriate hybridization conditions, e.g., typically higher salt and lower temperature, the probes will hybridize irrespective of imperfect complementarity. In fact, -with probes of greater than, e.g., about fifty nucleotides, the difference in stability of different sized probes will be relatively minor.

Applicant asserts that the '992 patent teaches that an isolated probe may be attached, but asserts that the patent does not actually teach the attachment of 50 nucleotide probe. Applicant asserts that by the '671 application cited in the '992 patent describes immobilization of anti-ligands e.g. oligonucleotides, but does not teach immobilization of probes having 50 nucleotides. From this, Applicant asserts that by the time of filing of the '992 patent, the Fodor group was using either VLSIPS or caged biotin, neither of which was actually used to produce an array having 50 nucleotide probes. The assertion is noted but is not found persuasive because the '992 patent cites the '671 application (column 27, lines 20-25) as teaching methods for attaching the probes (see below). The passage is cited for what it teaches and for what the '992 incorporates by reference. Hence, the citation is relevant for what it teaches i.e. probe attachment.

> In one embodiment, the individually isolated probes may be attached to the matrix at defined positions. These probe reagents may

be attached by an automated process making use of the caged biotin methodology described in Ser. No. 07/612,671,

It is maintained that the prior art, as cited above, anticipates the invention as claimed.

6. Claims 7, 9-15, 17-18, 21, 23-27, 29-32, 34-35, 38-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Winkler et al (U.S. Patent No. 5,677,195, filed 20 November 1992).

Regarding Claim 7, Winkler et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 400 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length (Column 17, lines 49-57 and Column 18, lines 47-50).

Regarding Claim 9, Winkler et al disclose the substrate wherein density is at least 2500 i.e. 10,000 regions/cm^2 (Column 18, lines 47-50)

Regarding Claim 10 Winkler et al disclose the substrate wherein the substrate is glass (Column 14, lines 45-46).

Regarding Claim 11 Winkler et al disclose the substrate wherein the substrate is non-porous i.e. glass (Column 14, lines 45-46).

Regarding Claim 12, Winkler et al disclose the substrate wherein the surface is hydrophobic (Column 9, lines 50-56 and Column 22, lines 8-20).

Regarding Claim 13, Winkler et al disclose the substrate wherein the surface comprises one or more functional groups e.g. silyl, hydroxyl, carboxyl, amine aldehyde, sulhydryl (Column 23, lines 13-18).

Regarding Claim 14, Winkler et al disclose the substrate wherein the DNA sequences are covalently bound (Column 10, lines 43-47).

Regarding Claim 15, Winkler et al disclose the substrate wherein the DNA sequences are non-covalently bound (Column 5, lines 42-47 and Column 10, lines 43-47).

Regarding Claim 17, Winkler et al disclose the substrate wherein the sequences are DNA sequences (Column 6, lines 18-22) that are comprised of nucleotides A, T, G, C. The claims are drawn to fragments of genomic DNA, which encompasses combinations of as few as two A, T, G, C. Because the claims are drawn to as few as two A, T, G and/or C and because Winkler et al teach 50mers of A, T, G and/or C. Winkler is deemed to teach the sequences as claimed.

Regarding Claim 18, Winkler et al disclose the substrate has at least 2500 or more regions i.e. 10,000/cm^2 (Column 18, lines 47-50).

Regarding Claim 21, Winkler et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 400 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length (Column 17, lines 49-57 and Column 18, lines 47-50). Winkler et al does not teach the method steps recited in the claim. However, the method steps do not result in any structural or compositional difference over the substrate of Winkler. Furthermore, as cited above, the courts have stated that the process of making a product does not distinguish the product over the prior art.

Regarding Claim 23, Winkler et al disclose the substrate wherein density is at least 2500 i.e. 10,000 regions/cm^2 (Column 18, lines 47-50)

Regarding Claim 24 Winkler et al disclose the substrate wherein the substrate is glass (Column 14, lines 45-46).

Regarding Claim 25 Winkler et al disclose the substrate wherein the substrate is non-porous i.e. glass (Column 14, lines 45-46).

Regarding Claim 26, Winkler et al disclose the substrate wherein the surface is hydrophobic (Column 9, lines 50-56 and Column 22, lines 8-20).

Regarding Claim 27, Winkler et al disclose the substrate wherein the surface comprises one or more functional groups e.g. silyl, hydroxyl, carboxyl, amine aldehyde, sulhydryl (Column 23, lines 13-18).

Regarding Claim 29, Winkler et al disclose the substrate wherein the DNA sequences are covalently bound (Column 10, lines 43-47).

Regarding Claim 30, Winkler et al disclose the substrate wherein the DNA sequences are non-covalently bound (Column 5, lines 42-47 and Column 10, lines 43-47).

Regarding Claim 31, Winkler et al disclose the substrate wherein the sequences are DNA sequences (Column 6, lines 18-22), which are, comprised of nucleotides A, T, G, C. The claims are drawn to fragments of genomic DNA that encompasses combinations of as few as two A, T, G, C. Because the claims are drawn to as few as two A, T, G and/or C and because Winkler et al teach 50mers of A, T, G and/or C. Winkler is deemed to teach the sequences as claimed.

Regarding Claim 32, Winkler et al disclose the substrate wherein density is at least 2500 i.e. 10,000 regions/cm^2 (Column 18, lines 47-50)

Regarding Claim 34, Winkler et al disclose (and claim) a substrate comprising a microarray of DNA having a density of 400 or more regions/cm^2 wherein the DNA sequences are about 50 subunits in length (Column 17, lines 49-57 and Column 18, lines 47-50). Winkler et al does not teach the method steps recited in the claim. However, the claimed selective hybridization is a recitation of intended use and, as cited above, the courts have stated that a recitation of intended use not distinguish a device over the prior art. Therefore, the detection does not further define the substrate.

Regarding Claim 35, Winkler et al disclose the substrate of Claim 34 but do not teach the detection as recited in the claim. However, the claimed detection is a recitation of intended use and the courts have stated that a recitation of intended use not distinguish a device over the prior art. Therefore, the detection does not further define the substrate of Claim 34.

Regarding Claim 38, Winkler et al disclose the substrate wherein the DNA is used to detect distinct sequences wherein relative binding is analyzed (e.g. Column 7, line 43-Column 8, line 7).

Regarding Claim 39, Winkler et al disclose the substrate wherein the DNA is used to detect distinct sequences wherein relative binding is analyzed (e.g. Column 7, line 43-Column 8, line 7).

Response to Arguments

7. Applicant asserts that the Winkler et al reference does not provide any enabling data that arrays of 50 nucleotides could be produced. Applicant argues that "the stated of the art at the time of the filing of Winkler et al (i.e., Nov, 1992) suggests that numerous inherent drawbacks of in situ synthesis including low coupling efficiency and premature truncation of a polymer limit the length of the synthesized polymers and their homogeneity." The arguments have been considered but are not found persuasive. As previously stated, Applicant has not provided any factual evidence of the asserted lack of enablement. Therefore, the assertion is deemed unsupported arguments of counsel. This is not to be considered an invitation for Applicant to submit a Declaration because a Declaration submitted after Final Action would not be deemed timely.

> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. (see (MPEP 716.01(c).

8. Claims 14, 29, 35, 38-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Pinkel et al (U.S. Patent No. 5,830,645, filed 9 December 1994).

The following rejection is based on the effective filing date for the claims as discussed above.

Regarding Claims 14, 29, 35, 38-39, Pinkel et al. teaches a microarray having DNA probe density of 1,000/cm^2 (Column 8, lines 61-62) and probe length of at least 50 (Column 4, lines 34-45) wherein the probes are covalently bound to the substrate (Column 8, lines 5-11) and wherein the array permits detection of relative abundance of polynucleotides and wherein the DNA sequences are distinct gene regions whose expression levels are related to differences between test and control cells (Column 6, lines 42-67).

Response to Arguments

9. As Applicant notes the dependent claims automatically carry the limitations of the independent claims. As such, Claim 14 as rejected above is drawn to the limitation of Claim 7 and Claim 14. The same is true for the other dependent claims.

Applicant asserts that Pinkel does not teach the instantly claimed invention because the nucleic acids of Pinkel differ from those claimed in that Pinkel does not teach at least 1,000 distinct targets/cm^2, each having at least 50 nucleotides and does not teach individually applied sequences. The assertion is noted but not found persuasive. As cited above, Pinkel specifically teaches probe density of 1,000/cm^2 (Column 8, lines 61-62) and probe length of at least 50 (Column 4, lines 34-45) and further teaches covalent attachment of the probes to the support (Columns 7-8). Applicant appears to be asserting that the term "complexity" used by Pinkel does not relate to probe length. It is noted that the reference uses the terms "kb" and "Mb" (i.e. kilobase and megabase) as a unit of measure. It is further noted that Claim 5 of Pinkel defines the nucleic acids as "about 1000 to about 1,000,000 nucleotides in complexity". Furthermore, Example 1 of Pinkel exemplifies probes of "ranging in length from several

hundred to over 10kb" (Column 13, lines 15-18). Hence, Pinkel clearly uses the term "complexity" to define the number of bases. Applicant points the passage at Column 8 wherein Pinkel describes arrays having densities greater than $10^4/cm^2$ and asserts that the reference is merely describing fluorescence detection, but not their arrays. The assertion is noted, but not found convincing. The reference is clearly describing known techniques useful for their arrays.

> Thus it is advantageous to have small array members that contain a small amount of concentrated target DNA so that the signal that is obtained is highly localized and bright. Such small array members are typically used in arrays with densities greater than 10.sup.4 /cm.sup.2. Relatively simple approaches capable of quantitative fluorescent imaging of 1 cm.sup.2 areas have been described that permit acquisition of data from a large number of members in a single image (see, e.g., Wittrup et. al. Cytometry 16:206-213 (1994)).

Applicant "believe" that Pinkel's teaching would not suggest the claimed invention because the working example uses control pore glass substrates not a high density array as claimed. The comment has been considered, but is not found persuasive because while the working example does not teach the array as claimed, working embodiment does not negate the other teachings of the patent e.g. arrays having densities greater than $10^4/cm^2$. The rejection is maintained.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 7, 9-18, 21, 23-27, 29-32, 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barrett et al (U.S. Patent No. 5,252,743, issued 12 October 1993) in view of Winkler et al (U.S. Patent No. 5,677,195, filed 20 November 1992).

Regarding Claims 7, 9-18, 21, 23-27, 29-32, 34-39, Barrett et al disclose a microarray (e.g. flat glass, Column 8, lines 25-27) having wherein the surface comprises isolated polynucleotides at a density of about 400 (10,000) regions/cm^2 (Column 20, lines 20-25, Example 1, and Fig. 4) wherein each region is formed by applying an aqueous reagent comprising the polynucleotide to a region that is uniformly hydrophobic (patterned) such that it prevents spreading of the reagent (i.e. the protecting groups lack affinity to specific binding substances, Column 14, lines 32-41) and wherein each region has a polynucleotide different from other regions (Column 2, lines 37-51).

Barrett et al further teach the substrate is glass (Column 8, lines 25-27), comprises functional groups for covalent or non-covalent attachment (Column 4, lines 45-52) and wherein the polynucleotides are greater than 1kD (Column 20, lines 45-47, 57). While the reference does not define subunit lengths as claimed (50 subunits), they exemplify large molecules (e.g. antibodies, Example P, Column 31) and they suggest immobilization of other various large molecules e.g. receptors, membrane transport proteins, glycoproteins (Column 20, lines 45-60) and clearly state that the immobilized molecules (e.g. oligonucleotides) are "typically greater than about 1kD" (Column 20, lines 45-47, 57). This clearly suggests oligonucleotides of at least 50 subunits. Furthermore, nucleic acid probes of at least 50 subunits were well known and preferred in the art at the time the claimed invention was made as taught by Winkler et al.

Winkler et al disclose (and claim) a similar substrate comprising a microarray of DNA having a density of 400 or more regions/cm^2 wherein the preferred DNA sequences are at least 50 subunits in length (Column 17, lines 49-57 and Column 18, lines 47-50).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the preferred probe lengths of Winkler et al to the probes of Barrett et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success based on the know and preferred lengths taught by Winkler et al (Column 17, line 57).

Barrett et al do not specifically teach the various species of oligonucleotides e.g. DNA, cDNA, RNA or mRNA. However, the genus of oligonucleotides is small such that the oligonucleotide species are obvious in view of a teaching of a genus. Therefore, the claimed DNA, cDNA, RNA or mRNA would have been obvious to one of ordinary skill in the art in view of the teaching of Barrett.

Response to Arguments

12. Applicant acknowledges that Barrett teaches oligonucleotides are anti-ligands and teaches immobilization of anti-ligands at predefined regions, but asserts that Barrett does not teach oligonucleotides of 50 nucleotides immobilized at the claimed density. Applicant asserts that the 500 μm x 500 μm checkerboard mask (Column 20, lines 20-25, Example I, and Fig. 4 and Column 29, lines 5-10) cited in the office action, does not define the overall size of the substrate and without knowledge of the substrate size, one cannot determine density. Applicant appears to be asserting that the claim requires a density of 1,000 or more probes per cm^2 over the entire surface of the substrate. However, the claims are not so limited. The claims merely require 1,000 or more probes at a density of 1,000 or more probes per cm^2. Applicant asserts that Barrett does not disclose any specific species of oligonucleotides and does not suggest probes of greater than 50 nucleotides. The assertion is noted, however as stated in the office action, Barrett suggests immobilization of other various large molecules and clearly state that the immobilized molecules (e.g. oligonucleotides) are "typically greater than about 1kD" (Column 20, lines 45-60). Furthermore, Applicant is reminded that the instant

rejection is an obviousness rejection wherein Winkler is relied upon for the suggestion of 50 nucleotide probes.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 7, 9-18, 21, 23-27, 29-32, 34-39 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 36-47 of copending Application No. 08/688,488. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a microarray substrate comprising DNA at a density of at least 400 regions/cm^2. The claims sets merely differ in the arrangement of limitations within the claim sets and minimal densities. The independent claims of the instant claim set defines a minimal density as 1,000 or more regions while the independent claim of the '488 application define a minimal density of 400 or more regions. The density ranges of both claim sets overlap i.e. at least 400 encompasses at least 1000 such that the instantly claimed range is a species of the '488 range.

The courts have stated that a genus is obvious in view of the teaching of a species see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). Therefore the instantly claimed range of at least 1,000 is obvious in view of the at least 400 recited in the '488 claims..

The claims sets further differ in the arrangement of limitations within the claim sets. The independent claim of the '488 application defines the substrate as hydrophobic, while dependent claims 10, 12, 16, 24, 26, 36 define the substrate as hydrophobic or comprises of a hydrophobic species. As such the instant claims are obvious in view of the '488 claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Comments

15. Applicant has not traversed the above rejection. The rejection is maintained.

Additional Comments

16. The claims may be placed in condition for allowance if:

1- the claims are amended to define a hydrophobic coating or surface material upon which the probes are spotted.

2- the claims are amended to define probes spotted onto the hydrophobic surface.

3- canceling claims drawn to covalent immobilization

4- filing of a terminal disclaimer over allowed application 08/688,488.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Primary Examiner
Art Unit: 1634
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